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Laparoscopic Cholecystectomy Versus Mini-Laparotomy Cholecystectomy

A Prospective, Randomized, Single-Blind Study

Axel Ros, MD,* Lennart Gustafsson, PhD,† Hans Krook, MD,‡ Carl-Eric Nordgren, MD,§ Anders Thorell, MD, PhD,‖ Göran Wallin, MD, PhD,‖ and Erik Nilsson, MD, PhD†

*From the Department of Surgery at *County Hospital of Ryhov, Jönköping, Sweden; †Motala Hospital, Motala, Sweden; ‡Vrinnevi Hospital, Norrköping, Sweden; §County Hospital, Kalmar, Sweden; and ‖Karolinska Hospital, Stockholm, Sweden.*

Objective

To analyze outcomes after open small-incision surgery (mini-laparotomy) and laparoscopic surgery for gallstone disease in general surgical practice.

Methods

This study was a randomized, single-blind, multicenter trial comparing laparoscopic cholecystectomy (LC) to minilaparotomy cholecystectomy (MC). Both elective and acute patients were eligible for inclusion. All surgeons normally performing cholecystectomy, both trainees under supervision and consultants, operated on randomized patients. LC was a routine procedure at participating hospitals, whereas MC was introduced after a short training period. All nonrandomized cholecystectomies at participating units during the study period were also recorded to analyze the external validity of trial results. The randomization period was from March 1, 1997, to April 30, 1999.

Results

Of 1,705 cholecystectomies performed at participating units during the randomization period, 724 entered the trial and 362 patients were randomized to each of the procedures. The groups were well matched for age and sex, but there were fewer acute operations in the LC group than the MC group. In the LC group 264 and in the MC group 150 operations were performed by surgeons who had done more than 25 operations of that type. Median operating times were 100 and 85 minutes for LC and MC, respectively. Median hospital stay was 2 days in each group, but in a nonparametric test it was significantly shorter after LC. Median sick leave and time for return to normal recreational activities were shorter after LC than MC. Intraoperative complications were less frequent in the MC group, but there was no difference in the postoperative complication rate between the groups. There was one serious bile duct injury in each group, but no deaths.

Conclusions

Operating time was longer and convalescence was smoother for LC compared with MC. Further analyses of LC versus MC are necessary regarding surgical training, surgical outcome, and health economy.

Changes in surgical technique, retrospectively recognized as being advantageous, have often been preceded by more than a decade of interest among devoted specialists before being introduced into surgical practice at large. Total mesorectal excision in the treatment of rectal cancer[1] and the use of mesh in hernia surgery[2,3] exemplify this. During the 1980s and in the early 1990s, it was shown that the conventional large subcostal incision in cholecystectomy could be replaced by a much smaller incision, giving a shorter convalescence.[4–6] This conclusion was later supported by results in three[7–9] out of four[7–10] randomized controlled trials. When laparoscopic cholecystectomy (LC) was introduced in the late 1980s, it rapidly became the dominant procedure for gallbladder surgery in the industrialized world. The main reason was that the new method was followed by a smoother postoperative course than conventional cholecystectomy.[11–13] LC has been found to take a longer time to perform and to cause less postoperative pain

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Correspondence: Axel Ros, MD, Department of Surgery, County Hospital of Ryhov, SE-55185 Jönköping, Sweden.
E-mail: axel.ros@telia.com
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than small-incision surgery, or minilaparotomy cholecystectomy (MC), whereas divergent results have been obtained with respect to hospital stay and convalescence.[14–18] The external validity (generalizability) of these studies is difficult to assess because with the exception of one study,[17] surgery was performed by specialist surgeons, trainees not being involved. Further, the surgeons may not have been equally familiar with the two techniques studied, and a difference in this respect is known to affect the outcome of a randomized trial.[19] It was therefore considered of interest to compare these two techniques in a routine healthcare situation (i.e., operations performed by junior surgeons under supervision as well as by consultants). The study should have an epidemiologic approach, taking into account all cholecystectomies in the observed population whether performed as part of the trial or not. The familiarity of surgeons with the methods studied should also be documented. We performed such a study as a randomized, single-blind, multicenter trial. We hypothesized that the postoperative courses after LC and MC would not differ significantly, and that LC would be more expensive when taking into account the overall cost to society.

PATIENTS AND METHODS

Participating Units, Study Period

Patients were randomized from March 1, 1997, to April 30, 1999. Participating units were the hospitals in Jönköping, Kalmar, Motala, and Norrköping, and the Karolinska Hospital in Stockholm. The latter hospital participated from Jan. 1, 1998, to Dec. 31, 1998, the other hospitals for the whole period. Ethics Committee approval was obtained for the study.

Recruitment of Patients

All patients advised to undergo a cholecystectomy, both elective and acute, were considered for inclusion. Exclusion criteria were age younger than 18 years, jaundice, obesity (body mass index > 45), pregnancy, cirrhosis of the liver, suspected or proven malignancy, and previous upper gastrointestinal tract surgery. The surgeon could also decide to exclude otherwise eligible patients if, for instance, surgical skill was not available for both procedures or if the patient was considered unsuitable for laparoscopy. Informed consent was obtained from each patient after verbal and written information was given.

Surgical Procedures

Since the early 1990s, LC had been practiced at participating hospitals. The study protocol gave no specific instructions on how to operate. Thus, each surgeon was free to choose the technique with which he or she felt comfortable. Conversion to open cholecystectomy was done when believed to be necessary and the reasons for conversion were registered. MC had been practiced to some extent in Jönköping before the study. After a workshop in October 1996, the procedure was introduced at the other hospitals between December 1996 and February 1997. It was defined as cholecystectomy performed through a laparotomy incision less than 8 cm long.[18] The surgeon could choose between a transverse subxiphoid incision and a short oblique one. Muscle splitting was allowed when considered necessary. Incision length and other technical details, such as the extent of muscle splitting, were recorded. If the skin incision was 8 cm or longer, reasons for the extension were registered.

The protocol stated that operative cholangiography should be attempted. Patients were anesthetized according to local hospital routine. Premedication included paracetamol or diclofenac. The protocol suggested that wounds and port sites should be infiltrated with bupivacaine. A nasogastric tube was used in all cases and removed immediately after surgery. An intraabdominal drain was left when considered necessary.

Both trainees under supervision and consultants operated on randomized patients. The experience of the operating surgeon and the assistant was recorded and dichotomized into two groups, 25 operations or less or more than 25 operations with the technique used.

Early oral intake and mobilization were encouraged. Patients were discharged according to hospital routines per the decision by the surgeon in charge. They were prescribed painkillers and were instructed to use them freely, and were encouraged to resume work and normal daily activity as soon as possible.

Randomization and Blinding

Randomization was done at each hospital using a "sealed envelope" technique. The envelopes were randomized in blocks of 18. The envelopes were drawn and opened by an operating room nurse not otherwise engaged in the study. Randomization was done just before surgery. Only operating surgeons and operating room staff were aware of the procedure performed. Wounds and port sites were dressed with identical opaque dressings regardless of surgical procedure. Operation documents were kept in a sealed envelope during the patient's hospital stay to keep the patient and ward personnel blind to the surgical procedure used.[18]

Data Collection and Processing

Preoperative, perioperative, and postoperative data for all cholecystectomies, randomized as well as nonrandomized, were recorded continuously according to protocol and later transferred to computer files at each hospital. Randomized patients answered questionnaires before surgery and 1 week, 1 month, and 1 year after the operation. The questionnaires included items concerning gastrointestinal symptoms, postoperative pain, time for return to work and normal

Table 1. PATIENTS

	Laparoscopy (n = 362)	Minilaparotomy (n = 362)	*P* Value
Age, mean (SD)	50.3 (15.1)	50.9 (16.1)	.62
Sex (male/female)	110/252	113/249	.80
Emergency/elective	43/319	63/299	.03
Body mass index, mean (SD)	27.3 (4.3)	26.6 (4.4)	.04
ASA 1-2/ASA 3-4	346/14	346/14	.32
Previous cholecystitis (yes/no)	72/290	64/298	.45
Previous pancreatitis (yes/no)	29/333	45/317	.05
Previous jaundice (yes/no)	14/348	41/321	<.001
Present cholecystitis (yes/no)	27/334	35/326	.29
Present pancreatitis (yes/no)	3/359	9/351	.08

daily activity, and overall and cosmetic satisfaction with the operation. They also included items concerning quality of life measurements according to the EuroQol protocol.[20] Endpoints were operating time, hospital stay, sick leave, intraoperative and postoperative complications, pain intensity, use of analgesics, and overall patient satisfaction with the procedure.

Interim analyses concerning differences between the two randomized groups were not undertaken. However, a control panel consisting of an experienced surgeon (Rolf Heuman, MD, PhD, and a statistician, Lennart Gustafsson, PhD) regularly performed such analyses without revealing the results to surgeons involved in the study. The control panel could also stop the trial in the event of unacceptable outcome differences between the randomized groups.

Data Validation

After compilation of data, several forms of controls were performed: logical control; random control of study protocols versus patient records; and control of all reported complications, reoperations, and bile duct injuries against patient records. Errors detected at these controls were corrected. To avoid printing errors, all data were fed into the computer twice.

Definitions

Acute cholecystitis was defined as gallstone according to ultrasound examination, abdominal pain, tenderness in the right upper quadrant, and a temperature of more than 38°C. Jaundice was defined as a serum bilirubin level more than twice the upper normal reference level. Pancreatitis was defined as abdominal pain and a serum amylase level more than twice the upper normal reference level. Any operation within 7 days of onset of persistent signs and symptoms of gallbladder disease was considered acute; all other operations were considered elective. Postoperative hospital stay was defined as the number of nights in the hospital after surgery plus nights during any readmission initiated within 30 days of surgery. In the original protocol, complications were classified on a three-level scale as none, minor, or serious, but after completion of the study we found this classification unsuitable. Therefore, after reading study protocols and patient records, all reported complications were reclassified as suggested by Clavien et al.[21]

Sample Size and Statistics

With a population of about 500,000 in the catchment area of the initially participating four hospitals, a cholecystectomy frequency of 130 per 100,000 inhabitants and calendar year, and an inclusion rate of 50% of patients undergoing cholecystectomy, 650 patients were expected to be included in the trial during a randomization period of 2 years. With a significance level of 5%, this sample size would have 95% power to detect a true mean difference between the two groups greater than one third of the standard deviation of normally distributed data. For binary data, a true difference of 10% or more between the two groups would be detected with a power of at least 80% for all proportions below 30%.

Data were analyzed according to the intent-to-treat principle. Hence, for the statistical analysis, converted laparoscopic operations were included in the laparoscopic group and open surgery with extended incision was included in the minilaparotomy group.

Outcome of a qualitative variable (e.g., use of analgesics [yes/no], postoperative complications [no/at least one]) was compared using chi-square analysis. The distribution of a quantitative variable (e.g., operating time, hospital stay) was compared by the Kolmogorov-Smirnov nonparametric two-sample test.

Possible effects of all significant differences between the groups in background factors (Table 1) on outcome variables were examined. Only differences in the frequency of acute operations and the experience of surgeons were found to influence quantitative variables. Operating time and hospital stay were therefore analyzed taking the frequency of acute operations and surgical experience into account. Adjusted analysis were performed (SPSS version 10) by a

Table 2. PROCEDURES

	Laparoscopy (n = 362)	Minilaparotomy (n = 362)	*P* Value
Infiltration anesthesia (yes/no)	269/79	296/52	.009
Intraoperative cholangiography done/tried/not done	314/7/40	334/1/27	
Drain (yes/no)	68/293	71/291	.78
Conversion-extended incision	69/293	101/261	<.001
CBD exploration (yes/no)	15/346	24/338	.14
Laparoscopic CBD–expl.	1		
Minilaparotomy CBD–expl.		3	
Open CBD–expl.	14	21	
T-tube drainage	15	21	.28
Intraoperative sphincterotomy	2	4	
Concomitant operations not related to cholecystectomy	5*	7†	

CBD, common bile duct.
* 3 liver biopsies, 2 umbilical hernias.
† 1 liver biopsy, 1 umbilical hernia, 1 hysterectomy, 1 hydrocele, 1 small bowel resection (not for cholecystectomy complication), 1 excision of a nevus, 1 liver resection (not for cholecystectomy complication).

three-way analysis of variance, model 3, with all interaction factors included.

Results are presented as numbers and percentages for the qualitative variables, with mean (SD) and median/quartiles for the quantitative ones. When appropriate, P values are given. $P \leq .05$ (two-tailed) was considered significant.

RESULTS

During the randomization period, 1,705 patients underwent a cholecystectomy. According to the exclusion criteria, 271 patients were not eligible for the study. Of 1,434 eligible patients, 726 (51%) were randomized. Two randomized patients were withdrawn; one had disseminated malignancy discovered at laparoscopy and the other patient was randomized to LC but operated on with MC for unclear reasons. Of the remaining 724 patients used for the statistical analysis, 362 were randomized to LC and 362 to MC. Among randomized patients, 106 of the 724 (14.6%) underwent acute operations, whereas the corresponding figures for the nonrandomized patients were 509 of 979 (52.0%, $P < .001$). Two hundred forty patients did not give consent for participation, 457 patients were excluded by the surgeon in charge (e.g., competence for both procedures was lacking, patient was considered unfit for laparoscopy), and 10 patients were excluded immediately before surgery (e.g., patient withdraw consent, anaesthesiologist did not accept patient for laparoscopy).

The groups were well matched except for the proportion of acute to elective procedures (LC, 43/319; MC, 63/299), previous history of jaundice and pancreatitis, and body mass index (see Table 1). Pre- and intraoperative procedures are presented in Table 2. Infiltration anesthesia of wounds was more frequently used in the MC group. Intraoperative cholangiography was successfully completed in 87% and 92% of the LC and MC group, respectively. Of all LCs, 69 (19%) were converted to open cholecystectomy and 101 (28%) of the MCs had an incision that exceeded 8 cm ($P < .01$). In five LCs and seven MCs, a concomitant procedure was performed that was not related to the cholecystectomy procedure; operating times for these procedures were included. Surgeons and assistants were more experienced in the laparoscopic technique. In 264 of the LCs, the surgeon had performed more than 25 LCs; the corresponding figure for MC was 150 ($P < .001$).

Mean operating times for the LC and MC groups were 108 ± 45 and 94 ± 45 minutes, respectively (Table 3). Taking differences in the experience of surgeons and mode of admission (acute vs. elective) into account, mean operating times were adjusted to 118 minutes (95% confidence interval [CI] 107–129) for LC and 93 minutes (86–100) for MC.

Intraoperative complications are presented in Table 4. There was at least one intraoperative complication in 134 (37%) LCs and 82 (23%) MCs ($P < .001$). Accidental puncture of the gallbladder (LC, 112/362; MC, 62/362) and stones left in the abdomen (LC, 10/362; MC, 0/362) were more frequent in LC. In one MC, the right hepatic artery was injured and was sutured with narrowing. In one LC, there was a small lesion of the liver caused by a trocar. None of these patients showed any signs of impaired postoperative liver function. Three cases of bowel injuries were

Table 3. OPERATION TIME

Operation Time (min)	Laparoscopy (n = 362)	Minilaparotomy (n = 362)
Mean (SD)	108 (45)	94 (45)
Median (lower–upper quartile)	100 (78–133)	85 (64–118)
	P < .001	

Table 4. INTRAOPERATIVE COMPLICATIONS (BILE DUCT INJURIES EXCLUDED)

Complications	Laparoscopy (n = 362)	Minilaparotomy (n = 362)
No	228	280
Yes, at least one	134	82
	$P<.001$	
Type of Complication		
Perforation of gallbladder	112	62
Bleeding	22	19
Stone left in abdomen	10	0
Vascular injury	0	1
Bowel injury	3	3
Hepatic injury	1	0

recognized in each group, of which two were penetrating in the LC group and one in the MC group. All these bowel injuries were recognized and repaired during surgery with an uneventful postoperative course.

There were no deaths in either group within 30 days of surgery. At least one postoperative complication was identified in 16.3% of LCs and 17.4% of MCs. Bile duct injuries and bile leaks excluded, there were eight serious complications (grade 2b or 3) per group (Table 5). Five patients in the LC group and four patients in the MC group had bleeding episodes requiring surgical or percutaneous drainage. One MC patient had postoperative pancreatitis treated with endoscopic sphincterotomy. Seven other cases of postoperative pancreatitis were treated conservatively. One MC patient had a myocardial infarction with uneventful recovery, and two MC patients had deep infection/abscess, one treated by percutaneous drainage and the other by surgical drainage. In the LC group one patient suffered a pneumothorax requiring drainage, and two patients were reoperated for incisional umbilical hernia.

Bile duct injuries and bile leaks occurred in six LC patients and seven MC patients (Table 6). There was one serious injury per group, with residual narrowing of the common bile duct in the LC patient and the left hepatic duct in the MC patient. At follow-up more than 1 year after their operation, these patients felt well and there were no signs of liver dysfunction. Two patients in the LC group had small lateral incisions in the common bile duct misinterpreted as the cystic duct. These injuries were discovered during cholangiography and easily managed. In two LC patients and six MC patients, invasive procedures were required to treat bile leaks.

Postoperative endoscopic retrograde cholangiography was undertaken in 15 patients per group (Table 7). Postoperative endoscopic sphincterotomy was performed in four LC and nine MC patients. Percutaneous drainage for bleeding, deep infection, or biloma was performed in three and six patients, respectively. Seven LC and 10 MC patients were reoperated. Six of these were MC patients operated for

Table 5. POSTOPERATIVE COMPLICATIONS BY TYPE AND SEVERITY

Postoperative Complication		1	2a	2b	3
Bleeding that required drainage	LC			5	0
(percutaneously/laparotomy)	MC			4	0
Postoperative pancreatitis	LC	1	1	0	0
	MC	1	4	1	0
Abdominal infection/abscess	LC	0	1	0	0
	MC	0	2	2	0
Superficial wound infection	LC	12	3	0	0
	MC	14	2	0	0
Pulmonary	LC	1	7	1	0
	MC	3	8	0	0
Kidney, urinary tract	LC	2	2	0	0
	MC	5	3	0	0
Cardiovascular	LC	0	1	0	0
	MC	0	4	0	1
Thromboembolism	LC	0	0	0	0
	MC	0	1	0	0
Central nervous system	LC	0	0	0	0
complications	MC	0	1	0	0
Other	LC	9	9	2	0
	MC	6	5	0	0

LC, laparoscopic cholecystectomy; MC, minilaparotomy.
All complications entered (i.e., one patient can have more than one complication in the table). Classified according to Clavien et al.[20] Bile duct injuries excluded; see Table 6.

bile leak (compared with no LC patients). However, two LC patients had a bile leak treated by endoscopic sphincterotomy and percutaneous drainage.

The figures given for hospital stay in Table 8 include readmission within 30 days of surgery. Mean hospital stay was slightly shorter after LC than MC: 2.6 and 3.2 days, respectively. Median time and lower and upper quartiles were identical for both groups at 2 (1 and 3) days. Conversion and extended incision prolonged the hospital stay in the LC and MC groups, respectively. For converted and not-converted LC, the hospital stay was 4.9 ± 3.7 days and 2.1 ± 4.9 days, respectively (95% CI for difference, 1.9–3.8 days). The hospital stay for MC with and without extended incision was 4.4 ± 4.4 days and 2.8 ± 5.3 days, respectively (95% CI for difference 0.5–2.7 days). Using a nonparametric test, the hospital stay was significantly longer for MC ($P = .04$). After adjusted analysis of variance for surgical experience and mode of admission, the hospital stay for LC and MC was 2.7 days (95% CI 1.6–3.8) and 3.5 days (95% CI 2.8–4.2), respectively. Mean and median sick leave, among those employed, was significantly shorter after LC than MC (12.7 and 16.0 days and 10 and 14 days, respectively), as was time for return to normal activities at home and to normal recreational activity ($P < .001$). One week after surgery, patients in the LC group had less pain and discomfort ($P < .001$), but after 1 month these differences had disappeared (Table 9). Patients in the LC group reported

Table 6. BILE DUCT INJURIES AND BILE LEAKS

	Laparoscopy	A	B
1	Transection with loss of substance in common bile duct detected postop., managed by primary suture and endoprosthesis, at follow-up residual narrowing	E1	III
2	Lateral incision in common bile duct detected intraop., managed by T-tube	D	IIb
3	Lateral incision in common bile duct in a converted laparoscopy detected intraop., managed by simple suture	D	IIb
4	Lateral incision in common bile duct detected intraop., managed by simple suture after conversion	D	IIb
5	Cystic leak detected postop., managed by endoscopic sphincterotomy and percutaneous drainage	A	IIb
6	Lap. chole. converted to open surgery due to stone in common duct, bile leak after extraction of T-tube drain, managed by endoscopic sphincterotomy		IIb
	Minilaparotomy		
7	Incision with loss of substance in left hepatic duct detected intraop., managed by primary suture and endoprosthesis. At follow-up residual narrowing of duct but symptom-free patient.	D	III
8	Bile leak from an accessory bile duct detected postop., managed by laparotomy drainage	A	IIb
9	Cystic leak detected postop., managed by laparotomy drainage	A	IIb
10	Bile leak of unclear origin detected postop., managed by laparotomy drainage	A	IIb
11	Cystic leak detected postop., managed by laparotomy drainage	A	IIb
12	Bile leak of unclear origin detected postop., managed by laparotomy drainage	A	IIb
13	Cystic leak detected postop., managed by laparotomy drainage	A	IIb

All bile duct injuries and complications detected during or after surgery.
A = Classification of bile duct injury according to Strasberg et al.[21]
B = Classification of complication according to Clavien et al.[20]

shorter pain duration during the first postoperative week (Fig. 1).

DISCUSSION

The aim of this study was to compare LC and MC in routine health care. Therefore, experienced surgeons as well as junior surgeons under supervision took part in the study. LC was already an established procedure at the participating hospitals, whereas MC was a new technique introduced after a workshop and a short training period. Thus, a significantly higher proportion of surgeons in the LC group had done more than 25 operations with the technique used. To our knowledge, this trial is the largest randomized one comparing LC and MC techniques. Both LC[13] and MC[9] have been shown to offer advantages over conventional large-incision cholecystectomy for patients with acute cholecystitis, and therefore acute cases were eligible for this study. Outside of specialized units, LC for acute cholecys-

Table 7. POSTOPERATIVE INTERVENTIONS

	Laparoscopy (n = 362)	Minilaparotomy (n = 362)	*P* Value
Cholangiography	15	22	.24
Endoscopic retrograde cholangiography	15	15	
Sphincterotomy	4	9	.16
Percutaneous drainage	3	6	
Reoperation	7	10	.47
Due to bleeding	4	3	
Due to bile leak	0	6	
Due to bile duct injury	1	0	
Due to other reason	2	1	

Table 8. HOSPITAL STAY AND CONVALESCENCE

	Laparoscopy (n = 362)	Minilaparotomy (n = 362)
Hospital stay, Readmissions within 30 days postop. are included.		
Mean ± SD, days	2.6 ± 3.3	3.2 ± 5.1
Median (lower–upper quartile)	2 (1–3)	2 (1–3)
	$P = .04$	
Sick leave (employed)	(n = 169)	(n = 170)
Mean ± SD, days	12.7 ± 10.3	16.0 ± 9.9
Median (lower–upper quartile)	10 (7–16)	14 (9–21)
	$P < .001$	
Return to normal activity at home	(n = 309)	(n = 301)
Mean ± SD, days	8.6 ± 7.7	10.7 ± 7.2
Median (lower–upper quartile)	6 (4–11)	8 (6–14)
	$P < .001$	
Return to normal recreational activity	(n = 268)	(n = 269)
Mean ± SD, days	11.5 ± 8.1	14.9 ± 8.9
Median (lower–upper quartile)	10 (5–14)	14 (8–20)
	$P < .001$	

Table 9. PAIN/DISCOMFORT

	Laparoscopy	Minilaparotomy
One Week Postop.	(n = 333)	(n = 341)
No pain/discomfort (%)	107 (32.1)	43 (12.6)
Moderate pain/discomfort (%)	214 (64.3)	280 (82.1)
Severe pain/discomfort (%)	12 (3.6)	18 (5.3)
	$P < .001$	
One Month Postop.	(n = 333)	(n = 328)
No pain/discomfort (%)	221 (66.4)	207 (63.1)
Moderate pain/discomfort (%)	107 (32.1)	115 (35.1)
Severe pain/discomfort (%)	5 (1.5)	6 (1.8)
	$P < .68$	

titis has been associated with a higher conversion[22,23] rate and a higher incidence of serious bile duct injuries[24] compared with elective operations. It is therefore not surprising to find a lower percentage of acute cases among our randomized patients compared with our nonrandomized patients. Like Majeed et al,[18] we blinded patients and ward personnel to the surgical procedure to avoid influence by their anticipation. Interim analyses were not performed to avoid multiple comparisons and expectation bias from surgeons.

The gallbladder was perforated more often and gallstones were lost and left in the abdomen more often in LCs. Bile spilling might cause local peritonitis, postoperative pain, and nausea, but whether these intraoperative complications have other implications is unclear. The study was not large enough to compare the low incidence of serious bile duct complications, but we recognized one such injury per group. There were two lateral incisions in the common hepatic duct misinterpreted as the cystic duct when preparing for intraoperative cholangiography. Strasberg et al[22] have questioned whether such incisions should be classified as complications. However, as pointed out by these authors, the common bile duct may have been dissected circumferentially and thereby devascularized before the incision, leading to later stricture development. There is also a gradual transition from a lateral incision to complete transection of a thin duct. Therefore, we think it appropriate to classify these lateral incisions as duct injuries. There were six bile leaks detected after surgery with MC versus two after LC. Three of the six leaks in the MC group were cystic duct leaks, underlining that great care is necessary in cystic duct closure.

There was no significant difference in the postoperative complication rate between the two groups. The complication rates were high compared with previous studies,[14–18] and we are concerned about our incidence of reoperation in comparison with data from units with a special interest in LC[25,26] or MC.[27] It is, however, difficult to compare negative outcomes of studies that use different classifications for complications. We used the classification proposed by Clavien et al,[21] in which grade 1 complications are minor. With these excluded, our complication rate was comparable to that in other controlled trials.

Operating time included time for cholangiography successfully performed in 87% and 92% of LC and MC procedures, respectively. Times were longer in this trial (median values 100 and 85 minutes for LC and MC) than in previous reports,[15–18] except in the trial by Kunz et al.[14] Wide inclusion criteria and participation of trainees, with resulting high conversion/extended incision rates, may have

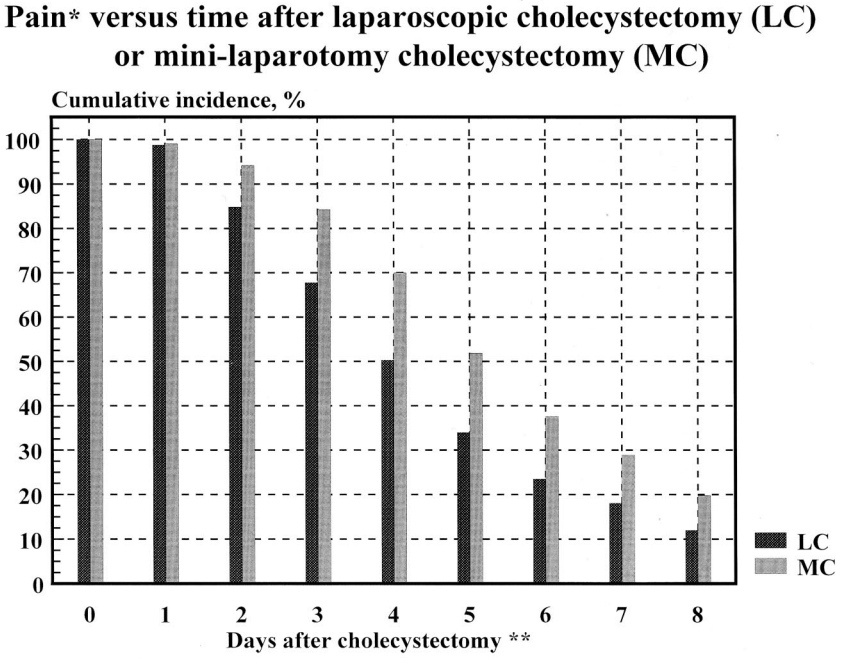

Figure 1. *Pain is defined as pain intensity of 3 or more on a visual analogue scale with no pain = 0 and maximum pain = 10. **Day of operation = 0.

contributed to our long operating times. The longer operating time for LC versus MC is in accordance with findings of previous randomized trials, with one exception,[14] and the mean difference in operating time was increased after adjustment for surgical experience and mode of admission. As pointed out by Majeed et al,[18] setting up and testing laparoscopic equipment usually add about 10 minutes to the procedure time.

Postoperative hospital stay in the present study included readmission. It was significantly longer for MC versus LC. However, the difference between means was small (0.6 nights), and after adjustment for surgical experience and mode of admission it did not reach statistical significance. Of three previous trials with 200 or more patients randomized, two trials found no difference in hospital stay between LC and MC when data were analyzed on an intent-to-treat basis,[17,18] whereas LC was associated with a shorter hospital stay in one trial.[16]

Sick leave and number of days required for return to normal activities at home and to recreational activities were significantly shorter after LC than after MC. Considerably longer sick leave was reported by McMahon et al[16] and by Majeed et al,[18] who found no difference between LC and MC patients. The study by McGinn et al[17] states data only for patients with "successfully completed" operations, whereas in reports by Barkun et al[15] and Kunz et al,[14] no data for return to work are given. Hence, differences in sick leave attributable to the two surgical techniques are far smaller than differences resulting from social circumstances and advice given to patients. Variations in medical attitudes toward the postoperative recovery period have also been shown to be a major determinant of sick leave.[28] As in other controlled trials, patients in the LC group had less pain for a shorter duration than patients in the MC group during the first postoperative week. Thus, the "no difference" hypothesis is rejected as far as convalescence is concerned. One month after surgery, however, no difference in perceived pain could be detected between the two groups. Postoperative recovery was also evaluated according to EuroQol quality of life variables. The results obtained concurred with data described above and will be presented in a forthcoming manuscript, together with a cost analysis of the study.

In conclusion, given the conditions of this study, LC took a longer time to perform and produced a slightly shorter postoperative hospital stay and a smoother postoperative course than MC. Trial outcome was affected by differences in surgical experience with the two techniques. Fewer intraoperative complications were recorded in the MC group. There was no difference in the postoperative complication rate between LC and MC, but the study was not designed to analyze serious complications. Health-care economy studies concerning gallbladder surgery and analyses of the incidence and outcome of cholecystectomy in defined populations are highly relevant.

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Discussion

PROF. A. JOHNSON: Congratulations on an excellent trial with large numbers—362 in each group, far bigger than any other such trial before. Personally I am delighted that you used our single-blind design in your trial. You have applied the philosophy of several trials that have been done in single centers with a few surgeons to the "real world" of teaching and district hospitals, including trainees. I am sure the figures that you give reflect what is happening in the average hospital around Europe. I think the inclusion of trainees does account for the longer operating time than in previous studies and perhaps for the conversion rate. You have been extremely honest in reporting your results, "warts and all." I have several questions.

If you found unexpected common bile duct stones at your operative cholangiograms, did you convert to open operation to remove them? The time off work in your study for both groups was considerably less than the other studies and we know this depends on the employment situation—whether patients are paid when they are off work or whether they have to get back to work to earn money. I would be interested to know whether you have analyzed the time off work by employment status. What methods did you use for pain relief, and how did you monitor it? Was it by patient-controlled analgesia, and did you use any local anesthetic techniques into the wounds or intercostal nerve blocks?

The learning curve is always in question when new techniques are being tried. Have you subanalyzed the data looking just at surgeons who have done over 25 minicholecystectomies, and have you subanalyzed just for elective operations because of the disparity in acute cholecystitis between the two groups?

My final question is a subjective one. Having seen minicholecystectomies, what do your nursing and medical staff think of it? Our own theater staff and junior doctors now prefer the minicholecystectomy, and most say they would have it if they had to have an operation themselves! I would be interested in the reaction of your teams.

PROF. F. HARDER: This is a very nice study with a good question, comparing the more complex setup in laparoscopic surgery with the simpler straightforward open surgery. I would like to draw your attention just to a few possible biases. The first, when you look at your slides, where you compare the several factors of biliary symptoms or biliary history of each patient, there are slightly more complications in the minilap group. There is a significantly larger number of emergency operations in the minilap group. Then there is a difference in specific surgical experience between the minilap surgeons and the laparoscopy surgeons. The minilap surgeons have considerably less routine in this type of surgery. Don't you think that these three elements (more complicated cases, more emergencies, less experience in the minilap group) could seriously influence the results and perhaps explain the extension of the small 8-cm incision in 28% of the cases?

Then of course, all the involved personnel in your hospital and the patients themselves must have known from the beginning what type of surgery they had. Could this also have an influence on pain medication or on hospital stay?

There is a small difference in operating time in favor of the minilap. But is this skin-to-skin or is it utilization of the OR, for that would only be relevant in the small observed difference? The setup of your laparoscopic instruments takes up time that needs to be added to the skin-to-skin time. The OR is certainly occupied for a longer time interval in the laparoscopic group then in the minilap group. Then, I think, in reality there will be no difference between the two groups in this respect.

PROF. D. J. GOUMA: I also enjoyed the trial very much; it is indeed the biggest trial ever done in this field. I still have some questions, however.

First of all, about 50% of the patients were not randomized in this study. There must be a reason. The randomization was shortly before surgery; could it be that in many of the nonrandomized patients there was no experience in the hospital to perform one of the procedures? Could you show the characteristics of patients not included in the study, and are they comparable with the characteristics of patients that were included?

The second question is that you aimed to evaluate the "effectiveness" of the procedure; that means that you should analyze the costs in relation to the quality of life. How did you calculate the sample size to look for the effectiveness, and what was the primary endpoint? You did not mention anything about the costs and costs reduction due to one of the procedures.

The hospital stay of laparoscopic cholecystectomy is shorter, there is an earlier recovery, and there is less pain. This is currently the most common procedure used in the world, so why should we now change for minilaparotomy? I do not see any reason to go back to the minilaparotomy, particularly because the conversion rate is quite high (30%).

The last question I have, and this is probably also a question for Prof. Johnson performing a previous trial: Do you really believe in blinding? If you put a trocar through the umbilicus instead of an incision of the right side of the abdomen, the patients will have pain at that location or are curious to look after the operation. So, is blinding really blinding in this procedure?

I enjoyed this study. Thank you.

PROF. E. NILSSON (CLOSING): Starting from the bottom line. Costs, we will report that later.

Sample size. It was set so that we could address all clinically relevant questions, except technique-related injuries, which will never be answered by randomized clinical trials.

Concerning the nonrandomized patients. There is one major difference between the randomized and the nonrandomized group, and that is the proportion of acute operations—15% and 52%, respectively. It is unethical to randomize every patient. You may not have competence available for both procedures, and some patients may be considered too sick for laparoscopy.

Operating time. It was shorter for minilaparotomy cholecystectomy. If you had added the time for setting up the equipment, the difference would have increased. As shown in our report, the difference also increased if you adjusted for surgical experience and for proportion of acute operations. Patients did not know what type of operation that had been done during hospital stay. (In fact, it was some kind of joke to keep this information hidden from the patients.) Of course, when they removed the dressing, they became aware of the procedures done.

Biases. Yes, we have biases. We are aware of the two that are mentioned in our report. There are more acute operations in the minilaparotomy group and surgical experience is less in this group. Those factors disfavor open surgery. The essence behind the randomized trial is not to create two groups exactly the same, but to test the null hypothesis, and for that you can adjust afterwards if you like. However, no adjustments will be made in the forthcoming cost analysis.

Staff reactions. It is very easy to tell: everyone is happy when an open operation is coming up now. As far as residents are concerned, they are very eager to do the small-incision open surgery. I think we have to reanalyze techniques of gallbladder surgery from an epidemiologic point of view. My personal view is that the winners of that reconsideration will be emergency cases now treated with conventional open surgery. They will be better off with the less traumatic minilaparotomy cholecystectomy.

As for the type of anesthesia, we used infiltration anesthesia in port sites and in the small-incision open surgery.

Employment. We have not analyzed that detail.

Common bile duct stones. There is experience but limited in Sweden of laparoscopic treatment of common bile duct stones. All except one of the common bile duct explorations in our trial were done openly in those groups.

Thank you very much.